

Notice of Allowability

Application No.

10/033,526

Applicant(s)

HUANG ET AL.

Examiner

Christopher Nichols, Ph.D.

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 3 December 2003.
2. ☒ The allowed claim(s) is/are 33-48.
3. ☒ The drawings filed on 02 November 2001 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
 - * Certified copies not received: _____.
5. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 - (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No. _____.
 - (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
 - (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the margin according to 37 CFR 1.121(d).

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|--|
| 1 <input type="checkbox"/> Notice of References Cited (PTO-892) | 5 <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2 <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6 <input checked="" type="checkbox"/> Interview Summary (PTO-413), Paper No. _____ |
| 3 <input checked="" type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No. _____ | 7 <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4 <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | 8 <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9 <input type="checkbox"/> Other |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Response and Amendment filed 3 December 2003 has been received and entered in full.
2. All previously made Objections and Rejections are hereby *withdrawn* in view of Applicant's acceptance of the Examiner's Amendment included herein.

EXAMINER'S AMENDMENT

3. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Claims 1-32 (Cancelled)

Claim 33 (Currently Amended) The method of claim + 39, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 28 kD to about 30 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

Claim 34 (Currently Amended) The method of claim + 39, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 14 kD to about 20 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

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Claim 35 (Currently Amended) The method of claim ~~23~~ 41, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 28 kD to about 30 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

Claim 36 (Currently Amended) The method of claim ~~23~~ 41, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 14 kD to about 20 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

Claim 37 (Currently Amended) The method of claim ~~32~~ 42, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 28 kD to about 30 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

Claim 38 (Currently Amended) The method of claim ~~32~~ 42, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 14 kD to about 20 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

Claim 39 (Previously Added) A method of inhibiting formation of neurofibrillary tangles in an individual, said method comprising:

administering to the individual a peptide that reduces formation of a neurotoxic carboxyl-terminal truncated form of apoE in a neuron in the individual, wherein the carboxyl-terminal truncated apoE comprises amino acids 244-260 of apoE, wherein the peptide is 4 to 6 amino acid residues in length, and wherein formation of neurofibrillary tangles is inhibited.

Claim 40 (Currently Amended) The method of claim 39, wherein the peptide is selected from the group consisting of Ala-Ala-Pro-Phe (SEQ ID NO: 1), Ala-Ala-Pro-Leu (SEQ ID NO: 3), and Ala-Ala-Ala-Ala-Pro-Phe (SEQ ID NO: 4).

Claim 41 (Previously Added) A method of inhibiting formation of neurofibrillary tangles in a neuronal cell of an individual, the method comprising:

contacting the neuronal cell with a peptide that inhibits an enzymatic activity of an enzyme in the neuronal cell that catalyzes cleavage of apoE in the cell to generate neurotoxic carboxyl-terminal truncated apoE, wherein the carboxyl-terminal truncated apoE comprises amino acids 244-260 of apoE, and wherein the peptide is 4 to 6 amino acid residues in length.

Claim 42 (Currently Amended) A method of reducing the level of carboxyl-terminal truncated apoE in a neuronal cell, the method comprising:

contacting the cell with a peptide that reduces activation of an enzyme that catalyzes the formation of neurotoxic carboxyl-terminal truncated apoE in a neuronal cell, wherein said enzyme is activated by $A\beta_{1-42}$, wherein the carboxyl-terminal truncated apoE comprises amino acids 244-260 of apoE, wherein the peptide is 4 to 6 amino acid residues in length, and wherein a reduction in the activation of the enzyme results in a reduction in the level of neurotoxic carboxyl-terminal truncated apoE in the cell.

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Claim 43 (Previously Added) A method of reducing formation of neurotoxic carboxyl-terminal apoE in a neuronal cell in an individual, the method comprising contacting the cell with a peptide that reduces formation of carboxyl-terminal truncated apoE in the individual, wherein the carboxyl-terminal truncated apoE comprises amino acids 244-260 of apoE, wherein the peptide is 4 or 5 amino acid residues in length, and wherein formation of neurotoxic carboxyl-terminal truncated apoE in the cell is reduced.

Claim 44 (Currently Amended) A method of treating Alzheimer's disease (AD), the method comprising administering a peptide selected from the group consisting of Ala-Ala-Pro-Phe (SEQ ID NO: 1), Ala-Ala-Pro-Leu (SEQ ID NO: 3), and Ala-Ala-Ala-Ala-Pro-Phe (SEQ ID NO: 4) in an amount effective to inhibit an enzyme that catalyzes the formation of carboxyl-terminal truncated apoE in a neuronal cell of an individual having AD, wherein the carboxyl-terminal truncated apoE comprises amino acids 244-260 of apoE, and wherein the enzyme is inhibited, and the level of carboxyl-terminal truncated apoE in a neuronal cell in the individual is reduced.

Claim 45 (New) The method of claim 43, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 28 kD to about 30 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

Claim 46 (New) The method of claim 43, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 14 kD to about 20 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

Claim 47 (New) The method of claim 44, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 28 kD to about 30 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

Claim 48 (New) The method of claim 44, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 14 kD to about 20 kD as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis analysis.

4. An extension of time under 37 CFR 1.136(a) is required to place this application in condition for allowance. During a telephone conversation conducted on 15 January 2004, Paula Borden requested an extension of time for 2 MONTH(S) and authorized the Director to charge Deposit Account No. 50-0815 the required fee of \$475.00 for this extension.

5. Authorization for this examiner's amendment was given in a telephone interview with Paula Borden (Reg. No. 42,344) on 15 January 2004.

Summary

6. Claims 33-48 are hereby allowed.

7. The Examiner acknowledges that acceptance of the above Examiner's Amendment does not mitigate in any way, shape, or form, Applicant's right to pursue additional subject matter in continuation, continuation-in-part, and/or divisional applications pursuant to 35 U.S.C. §120 and §121.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
January 15, 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER